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Association Between Cardiac Catheterization Laboratory Pre-Activation and Reperfusion Timing Metrics and Outcomes in Patients With ST-Segment Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention

A Report From the ACTION Registry

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ABSTRACT

OBJECTIVES The aim of this study was to describe the prevalence of pre-hospital cardiac catheterization laboratory activation and its association with reperfusion timeliness and in-hospital mortality.

BACKGROUND For patients with ST-segment elevation myocardial infarction diagnosed in the field, catheterization laboratory pre-activation may lead to more timely reperfusion and improved outcomes.

METHODS A total of 27,840 patients with ST-segment elevation myocardial infarction transported via emergency medical services to 744 percutaneous coronary intervention–capable hospitals in the ACTION Registry from January 2015 to March 2017 were evaluated, excluding patients with cardiac arrest or requiring pre-percutaneous coronary intervention intubation. Catheterization laboratory pre-activation was defined as activation >10 min prior to hospital arrival.

RESULTS Catheterization laboratory pre-activation occurred in 41% of patients (n = 11,379), with minor presenting differences between those with and without catheterization laboratory pre-activation. Compared with no catheterization laboratory pre-activation, pre-activation patients were more likely to be directly transported to the catheterization laboratory on hospital arrival (23.3% vs. 5.3%), to have shorter hospital arrival-to-catheterization laboratory arrival time (median 17 min [interquartile range (IQR): 7 to 25 min] vs. 28 min [IQR: 18 to 39 min]), to have shorter door-to-device time (40 min [IQR: 30 to 51 min] vs. 52 min [IQR: 41 to 65 min]), and to have a greater likelihood of achieving first medical contact–to-device time ≤90 min (76.6% vs. 68.6%) ($p < 0.001$ for all). Pre-activation was associated with lower in-hospital mortality (2.8% vs. 3.4%; $p = 0.01$). Patients treated at hospitals in the lowest tertile of pre-activation rates had higher mortality than those treated at hospitals in the highest tertile before and after adjustment (3.6% vs. 2.7%; adjusted odds ratio: 1.33; 95% confidence interval: 1.08 to 1.63).

CONCLUSIONS In the United States, catheterization laboratory pre-activation occurred in fewer than one-half of emergency medical services–transported patients with ST-segment elevation myocardial infarction. Its association with faster reperfusion and lower mortality supports greater use of this strategy. (J Am Coll Cardiol Intv 2018;11:1837–47)

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ABBREVIATIONS AND ACRONYMS

CI = confidence interval

EMS = emergency medical services

FMC = first medical contact

IQR = interquartile range

OR = odds ratio

PCI = percutaneous coronary intervention

STEMI = ST-segment elevation myocardial infarction

In ST-segment elevation myocardial infarction (STEMI), pre-hospital cardiac catheterization laboratory activation offers the opportunity to facilitate more rapid primary percutaneous coronary intervention (PCI) by improving catheterization laboratory readiness prior to patient arrival (1,2). However, integrated treatment protocols are needed between PCI-capable hospitals and pre-hospital emergency medical services (EMS) providers to facilitate and successfully implement catheterization laboratory pre-activation strategies (3,4). We hypothesize that there is substantial underuse and between-hospital variability in the nationwide use of catheterization laboratory pre-activation, as has been observed in the implementation of other pre-hospital processes of STEMI care, such as the use of pre-hospital electrocardiography and emergency department bypass protocols (4-7). The associations between catheterization laboratory pre-activation and reperfusion timing and clinical outcomes have been poorly characterized.

Therefore, we evaluated the National Cardiovascular Data Registry ACTION (Acute Coronary Treatment and Intervention Outcomes Network) Registry to describe the use of and interhospital variability in catheterization laboratory pre-activation for patients diagnosed with STEMI in the field and transported by EMS to PCI-capable hospitals. We then evaluated the association of catheterization laboratory pre-activation with reperfusion timing metrics and in-hospital mortality.

METHODS

DATA SOURCE AND STUDY POPULATION. Details of the ACTION Registry have been previously described (8). In brief, the ACTION Registry is a large, ongoing, voluntary quality improvement initiative sponsored by the American College of Cardiology and American Heart Association that includes consecutive patients admitted to participating hospitals with STEMI or non-ST-segment elevation myocardial infarction. Trained data abstractors collect detailed inpatient data for patients with acute myocardial infarction using a standardized set of data elements and definitions (available at https://www.ncdr.com/webncdr/action/home/datacollection). Data quality assessment has demonstrated chart review agreement of >93% of collected variables (9). For all participating sites, registry participation was approved by an Institutional Review Board.

The time of catheterization laboratory activation was collected by the ACTION Registry beginning January 1, 2015. Our study population comprised 39,026 pre-hospital-identified patients with STEMI treated with primary PCI from January 1, 2015, to March 31, 2017. The following exclusions were sequentially applied (**Figure 1**): patients who transferred to an ACTION hospital from another hospital (n = 1,497) or who first arrived to a non-PCI-capable hospital (n = 160); patients with cardiac arrest on first medical contact (FMC) (n = 2,934); those with non-system-related PCI delays due to medical needs such as intubation (n = 1,200); those transported by self, family, or air ambulance (n = 1,355); those with FMC-to-device times ≥240 min (n = 632); and patients among whom the catheterization laboratory was activated either 60 min prior to or after hospital arrival (n = 123). These criteria excluded selected patients who may have had unmeasured confounding characteristics leading to very early or very late catheterization laboratory activation. Last, patients with missing catheterization laboratory activation times (n = 3,285) were also excluded. The final study population consisted of 27,840 patients with STEMI treated with primary PCI at 744 PCI-capable hospitals in the United States.

DEFINITIONS. FMC indicates the time at which the patient was first evaluated by EMS personnel prior to arrival at the PCI-capable hospital. Device activation reflects the earliest time the first device was activated or deployed after wire crossing (balloon, stent, or an adjunct PCI device such as an aspiration thrombectomy catheter). The "door" time indicates the time at first arrival to the PCI-capable hospital. Detailed references to these definitions are available in the ACTION Registry Coder's Data Dictionary (https://www.ncdr.com/webncdr/action/home/datacollection). Catheterization laboratory pre-activation was defined

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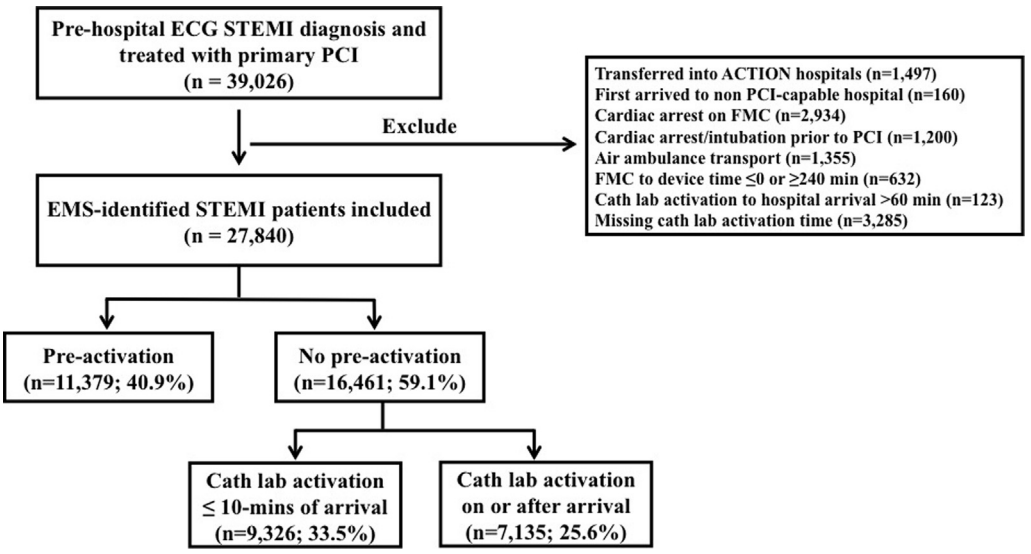
FIGURE 1 Derivation of the Study Sample and Cardiac Catheterization Laboratory Pre-Activation Relative to Hospital Arrival



ACTION = Acute Coronary Treatment and Intervention Outcomes Network; ECG = electrocardiographic; EMS = emergency medical services; FMC = first medical contact; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.

as an alert (or activation) by EMS occurring >10 min prior to arrival at the receiving PCI-capable center. Any call to activate the catheterization laboratory occurring ≤10 min prior to or on or after hospital arrival at the PCI center was defined as no catheterization laboratory pre-activation. This 10-min notification window in defining catheterization laboratory pre-activation was based on a clinically determined reasonable amount of advanced notification required to prepare the catheterization laboratory and its staff to significantly influence reperfusion timing. Shorter notification times prior to patient arrival offer little opportunity to mitigate reperfusion delays. Furthermore, STEMI guidelines have used 10-min benchmarks for other STEMI processes of care, such as time from FMC to electrocardiography and time to fibrinolysis in anticipated primary PCI delays (10,11). Our use of a >10-min catheterization laboratory notification before hospital arrival thus factors in the rationale for catheterization laboratory pre-activation and aligns with a time window in which its use may be associated with significant time savings. The ACTION Registry does not collect information pertaining to catheterization laboratory activation in patients who were ultimately not diagnosed with STEMI (false catheterization laboratory activations). However, as the scope of this analysis was to detail the association between catheterization laboratory pre-activation and its relationship with reperfusion timings and in-hospital outcomes, this analysis represents "true" patients with STEMI, all treated with primary PCI.

STATISTICAL ANALYSIS. We compared baseline presenting characteristics, reperfusion timings, and in-hospital outcomes by catheterization laboratory pre-activation status using chi-square and Wilcoxon rank sum tests for categorical and continuous variables, respectively. Categorical variables are reported as percentages and continuous variables as medians with interquartile ranges [IQRs].

Because catheterization laboratory pre-activation principally aims to reduce in-hospital treatment delays by either shortening the time spent within the emergency department or entirely bypassing it, our primary objective was to evaluate the relationship between catheterization laboratory pre-activation and door-to-device time. Additionally, we aimed to explore how notification times relate to in-hospital treatment delays and thus evaluated door-to-device time by catheterization laboratory activation-to-hospital arrival time in 10-min increments (except for the tail ends of the data, which had >10 min of increment). As secondary objectives, we compared FMC-to-device times and the proportion of patients achieving FMC-to-device times of ≤90 min by catheterization laboratory pre-activation status.

TABLE 1 Baseline and In-Hospital Characteristics Categorized by Cardiac Catheterization Laboratory Pre-Activation

	Overall (N = 27,840)	Catheterization Laboratory Pre-Activation		p Value
		Yes (n = 11,379)	No (n = 16,461)	
Patient characteristics				
Age, yrs	62 (54–71)	62 (54–71)	62 (54–71)	0.73
Male	70.5	70.7	70.4	0.55
BMI, kg/m^2	28.3 (25.1–32.3)	28.4 (25.1–32.3)	28.2 (25.1–32.2)	0.06
Race				<0.001
White	80.2	83.3	78.0	
Black	9.7	7.8	11.1	
Asian	3.0	2.9	3.1	
Hispanic	6.0	4.7	6.9	
Other	0.5	0.6	0.5	
Risk profiles				
Current/recent smoker (<1 yr)	40.6	40.4	40.7	0.63
Hypertension	63.9	62.4	65.0	<0.001
Diabetes	24.6	23.9	25.1	0.02
Prior MI	15.8	15.0	16.4	0.001
Prior revascularization	20.8	19.9	21.4	0.002
Prior heart failure	3.5	3.3	3.7	0.06
Cerebrovascular disease	7.1	6.7	7.3	0.08
Peripheral arterial disease	4.2	4.0	4.3	0.21
Presenting profiles				
Off-hour presentation*	57.6	56.8	58.1	0.04
Heart failure at presentation	4.0	3.7	4.2	0.03
Cardiogenic shock	5.0	5.0	5.0	0.75
Systolic blood pressure, mm Hg	138 (116–160)	138 (117–160)	137 (115–160)	0.03
Heart rate, beats/min	76 (63–90)	76 (62–90)	76 (63–90)	0.15
ACTION in-hospital mortality risk score	32 (26–39)	32 (26–39)	32 (26–39)	0.16
In-hospital characteristics				
Ejection fraction				0.004
>50%	55.5	56.6	54.8	
40%–50%	24.8	24.6	25.0	
25%–40%	16.3	15.8	16.7	
<25%	3.3	3.0	3.5	
Medications within 24 h				
Aspirin	99.2	99.3	99.1	0.02
P2Y$_{12}$ inhibitor	96.7	96.9	96.5	0.07
ACE inhibitor or ARB	50.2	50.3	50.1	0.69
Beta-blocker	86.3	86.7	86.0	0.13
Statin	83.3	84.0	82.9	0.03

Values are median (interquartile range) or %. *In this study, work-hour presentations were defined as hospital arrival during weekdays (Monday to Friday, 7 AM to 6 PM); off-hour presentations were defined as hospital arrival during weeknights (Monday to Friday, 6 PM to 7 AM), weekdays, and holidays including New Year's Eve and New Year's Day (December 31 and January 1), Christmas Eve and Christmas Day (December 24 and 25), Memorial Day (relevant calendar dates for 2015 to 2017), Independence Day (July 4), Labor Day (relevant calendar dates for 2015 to 2017), and Thanksgiving (Wednesday after 6 PM through Monday before 7 AM).

ACE = angiotensin-converting enzyme; ACTION = Acute Coronary Treatment and Intervention Outcomes Network; ARB = angiotensin receptor blocker; BMI = body mass index; MI = myocardial infarction.

Furthermore, because catheterization laboratories are generally not staffed 24/7, pre-activation is likely to have differential time-to-treatment effect dependent on the time of day the patient presents to the hospital. Therefore, we profiled the relationships between catheterization laboratory pre-activation and door-to-device and FMC-to-device times by patient hospital arrival during work hours versus off hours.

To determine the association between catheterization laboratory pre-activation and in-hospital mortality, patients who transferred out of ACTION Registry hospitals were excluded, because their clinical outcomes could no longer be determined (n = 616). We used logistic generalized estimating equations regression with an exchangeable working correlation matrix to account for within-hospital clustering of outcomes. This methodology produces estimates that are similar to those from logistic regression with variances that are adjusted for the correlation of outcomes within a hospital (12). The list of covariates was from the previously validated and published ACTION Registry in-hospital mortality model (13) and based on our collective clinical judgment (Online Table 1). Adjusted odds ratios (ORs) for in-hospital mortality and 95% confidence intervals (CIs) were reported by catheterization laboratory pre-activation status.

For analyses exploring hospital-level variation for use of catheterization laboratory pre-activation, patients admitted to hospitals with ≤20 patients with STEMI during the study period were excluded (n = 2,803; 281 hospitals) in order to focus only on hospitals with adequate STEMI volume. Hospitals were sorted by proportions of catheterization laboratory pre-activation and divided into 3 groups: low, intermediate, and high tertiles. Hospitals in the low-tertile group had the smallest proportion of patients who received catheterization laboratory pre-activation. Patient baseline characteristics, treatment patterns, reperfusion timing metrics, in-hospital mortality, and hospital characteristics were stratified by tertiles of hospital-specific use of catheterization laboratory pre-activation. We additionally evaluated, across the tertiles of catheterization laboratory pre-activation, hospital performance measured using the American College of Cardiology/American Heart Association defect-free care score. Briefly, the defect-free care score reflects the proportion of patients treated at a hospital with perfect adherence to the guideline metrics among all eligible care opportunities for the following guidelines metrics: hospital arrival-to-primary PCI time ≤90 min, evaluation of left ventricular systolic function, aspirin on arrival and at discharge, discharge use of statin, beta-blocker, angiotensin-converting enzyme inhibitor, or angiotensin receptor blocker for systolic function ≤40%, smoking cessation counseling, and cardiac rehabilitation referral (14,15). Chi-square and Kruskal-Wallis tests were used to compare categorical and continuous variables, respectively. In addition, we evaluated the association between hospital use of catheterization laboratory pre-activation and

in-hospital mortality using generalized estimating equations logistic regression, adjusting for the same covariate list (Online Table 1). Last, the percentage of missingness for each covariate was approximately 1% to 2%; therefore, missing values in continuous covariates were imputed to the sex-specific median of the nonmissing values, and missing values in categorical covariates were imputed to the most frequent group. A p value of <0.05 was considered to indicate statistical significance for all analyses. All statistical analyses were performed using SAS version 9.4 software (SAS Institute, Cary, North Carolina).

RESULTS

Among the 27,840 eligible patients with STEMI, catheterization laboratory pre-activation >10 min occurred in 40.9% (n = 11,379). A total of 9,326 patients (33.5%) had notification of the catheterization laboratory ≤10 min prior to hospital arrival, and the remaining 7,135 patients (25.6%) had catheterization laboratory activation on or after hospital arrival (Figure 1). Baseline patient profile, treatment patterns, and hospital-level characteristics by catheterization laboratory pre-activation status (pre-activation vs. not) are described in Table 1. Both groups appear to be largely similar except that patients with pre-activation were more likely to be white.

TABLE 2 Reperfusion Measures Stratified by Cardiac Catheterization Laboratory Pre-Activation

	Pre-Activation (n = 11,379)	No Pre-Activation (n = 16,461)	p Value
Overall			
Direct arrival to catheterization laboratory	23.3	5.3	<0.001
FMC to hospital arrival (min)	34 (27–43)	26 (21–33)	<0.001
FMC to ECG (min)	5 (3–9)	6 (3–10)	<0.001
ECG to catheterization laboratory activation (min)	9 (4–15)	17 (10–28)	<0.001
ECG to hospital arrival (min)	27 (21–37)	19 (13–26)	<0.001
Door to device (min)	40 (30–51)	52 (41–65)	<0.001
Hospital arrival to catheterization laboratory arrival (min)	17 (7–25)	28 (18–39)	<0.001
Catheterization laboratory arrival to device activation (min)	22 (17–29)	23 (17–29)	<0.001
FMC to device (min)	76 (64–89)	80 (66–95)	<0.001
FMC to device ≤90 min	76.6	68.6	<0.001
Off-hour presentation			
Direct arrival to catheterization laboratory	12.2	2.1	<0.001
Door to device (min)	45 (36–56)	58 (49–69)	<0.001
FMC to device (min)	81 (71–94)	86 (74–101)	<0.001
FMC to device ≤90 min	69.2	58.6	<0.001
Work-hour presentation			
Direct arrival to catheterization laboratory	38.0	9.8	<0.001
Door to device (min)	33 (24–43)	42 (33–53)	<0.001
FMC to device (min)	68 (57–81)	69 (58–84)	<0.001
FMC to device ≤90 min	86.3	82.4	<0.001

Values are % or median (interquartile range). FMC is defined as the time at which the patient was first evaluated by EMS personnel. Device activation reflects the earliest time the first device (balloon, stent, or an adjunct PCI device such as an aspiration thrombectomy catheter) was deployed after wire crossing. "Door" time indicates the time at first arrival to the PCI-capable hospital.

ECG = electrocardiography; FMC = first medical contact; PCI = percutaneous coronary intervention.

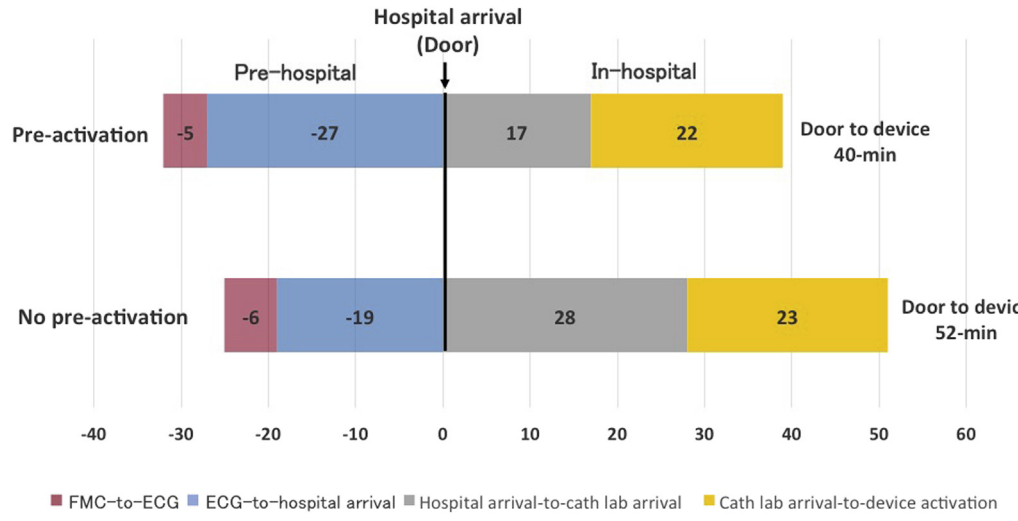
REPERFUSION TIMING. The distribution of the door-to-device times for patients in whom catheterization laboratory activation occurred >10 min prior to hospital arrival, ≤10 min before hospital arrival, and on or after hospital arrival are as follows: median 40 min (IQR: 30 to 51 min) versus 48 min (IQR: 37 to 59 min) versus 59 min (IQR: 46 to 71 min), respectively (p < 0.001 for all groups).

Catheterization laboratory pre-activation was associated with a median 12-min shorter door-to-device time and a higher proportion of patients achieving FMC-to-device times of ≤90 min (76.6% vs. 68.6%; p < 0.001) compared with no catheterization laboratory pre-activation (Table 2). In part, this was because pre-activation was also associated with a greater proportion of patients being directly transported to the catheterization laboratory on hospital arrival compared with those among whom the catheterization laboratory was not pre-activated (23.3% vs. 5.3%; p < 0.001) (Table 2). This association was observed in patients who presented both during working hours and during off hours. Pre-activated patients also spent shorter time in the emergency department (hospital arrival to catheterization laboratory arrival: median 17 min [IQR: 7 to 25 min] vs. 28 min [IQR: 18 to 39 min]); p < 0.001) (Figure 2). The longer the amount of advance notification received (catheterization laboratory activation to hospital arrival time), the higher the likelihood of shorter door to device times (Figure 3).

IN-HOSPITAL EVENTS. The observed in-hospital mortality rate was lower with catheterization laboratory pre-activation compared with no pre-activation (2.8% vs. 3.4%; p = 0.012). Following risk adjustment, this association was no longer statistically significant (OR: 0.87; 95% CI: 0.75 to 1.01). Catheterization laboratory pre-activation was not associated with a difference in the incidence of heart failure (5.3% vs. 5.1%; p = 0.41) or cardiogenic shock (5.8% vs. 6.1%; p = 0.26) compared with no pre-activation.

HOSPITAL-LEVEL VARIABILITY. Of the 463 eligible hospitals evaluated, we observed significant inter-hospital variability in the rate of catheterization laboratory pre-activation (Figure 4). The median pre-activation rate was 38% (IQR: 25% to 53%), and rates for each hospital tertile were as follows: low, 19% (IQR: 11% to 25%); intermediate, 38% (IQR: 35% to 43%); and high, 58% (IQR: 52% to 68%). Low-tertile

FIGURE 2 Treatment Times Categorized by Cardiac Catheterization Laboratory Pre-Activation Treatment Times Described as Medians



ECG = electrocardiography; FMC = first medical contact.

hospitals were more likely to be urban, academic teaching hospitals and to have lower annual STEMI volumes compared with intermediate-tertile and high-tertile hospitals. Comparable defect-free care scores were noted across the tertiles of catheterization laboratory pre-activation (**Table 3**).

Low-tertile hospitals (vs. intermediate vs. high) had a significantly smaller proportion of patients who were first evaluated in the catheterization laboratory (4.1% vs. 10.1% vs. 22.4%; $p < 0.001$) (Online Table 2). Patients presenting to low-tertile (compared with intermediate-tertile and high-tertile) hospitals also had significantly longer door-to-device times and smaller proportions of patients achieving FMC-to-device times of ≤90 min (**Table 4**). Patients arriving at low-tertile hospitals (vs. intermediate-tertile vs. high-tertile) had the highest unadjusted rate of in-hospital mortality (3.6% vs. 3.1% vs. 2.7%; $p = 0.005$). Following risk adjustment, patients in low- versus high-tertile hospitals still had higher in-hospital mortality (OR: 1.33; 95% CI: 1.08 to 1.63); however, a similar association was not evident for patients presenting to low- versus intermediate-tertile catheterization laboratory pre-activation hospitals (OR: 1.09; 95% CI: 0.88 to 1.33).

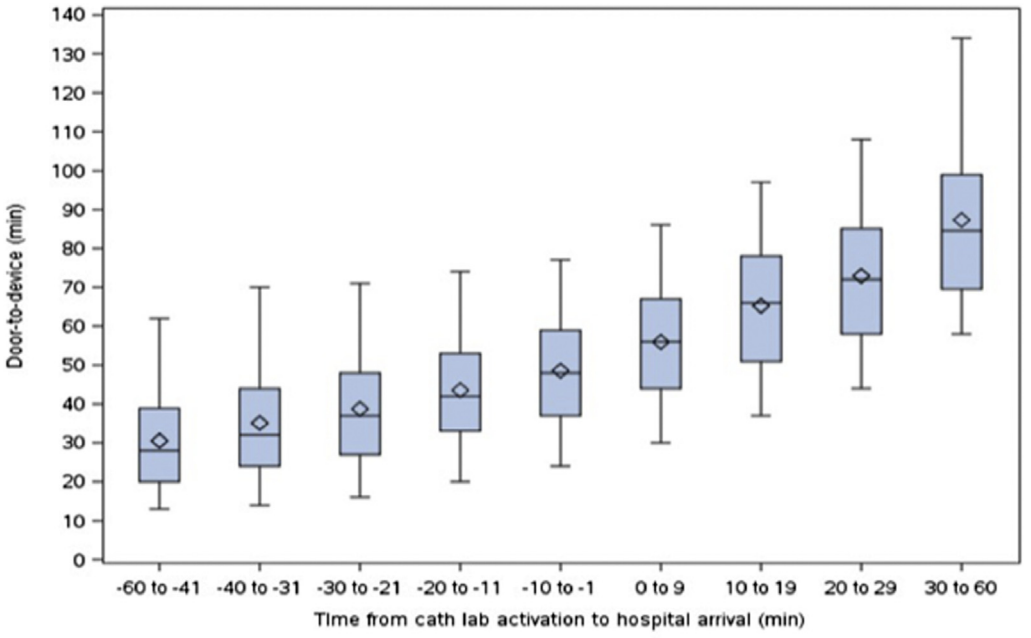
DISCUSSION

Our analysis profiling catheterization laboratory pre-activation in contemporary U.S. practice reveals the following key findings: 1) 41% of pre-hospital-identified patients with STEMI undergoing PCI had catheterization laboratory pre-activation ≥10 min before hospital arrival; 2) pre-activation was associated with a significantly lower likelihood of reperfusion delay for patients presenting during both work hours and off hours; and 3) hospitals with higher rates of pre-activation had lower risk-adjusted in-hospital mortality compared with hospitals with lower pre-activation rates.

Optimal pre-hospital STEMI care includes rapid electrocardiographic acquisition and communication of a STEMI diagnosis to the nearest primary PCI center. Expedited catheterization laboratory pre-activation is thus a key element in reducing primary PCI-related delays (10,11). Broad descriptions in regional and nationwide representative samples have previously associated catheterization laboratory pre-activation with median door-to-device times that were 10 to 15 min shorter (6,7,16–18). However, limited granular data exist on how advanced catheterization laboratory notification is associated with primary PCI-related reperfusion delays and in-hospital outcomes.

Our findings therefore seek to expand on prior analyses by highlighting several unique findings. First, demonstrating the timing of catheterization laboratory activation in relation to hospital arrival provides a contemporary perspective on U.S. catheterization laboratory activation practice patterns. We

FIGURE 3 Relationship Between Time From Cardiac Catheterization Laboratory Activation to Hospital Arrival and Door-to-Device Time



Each **box** represents the door-to-device time. The **line and the diamond within the box** represent the median and mean times, respectively; the **bottom and top ends of the box** represent the 25th and 75th percentiles, and the **whiskers** represent the 5th and 95th percentiles.

FIGURE 4 Distribution of Hospital-Level Variability in Use of Cardiac Catheterization Laboratory Pre-Activation

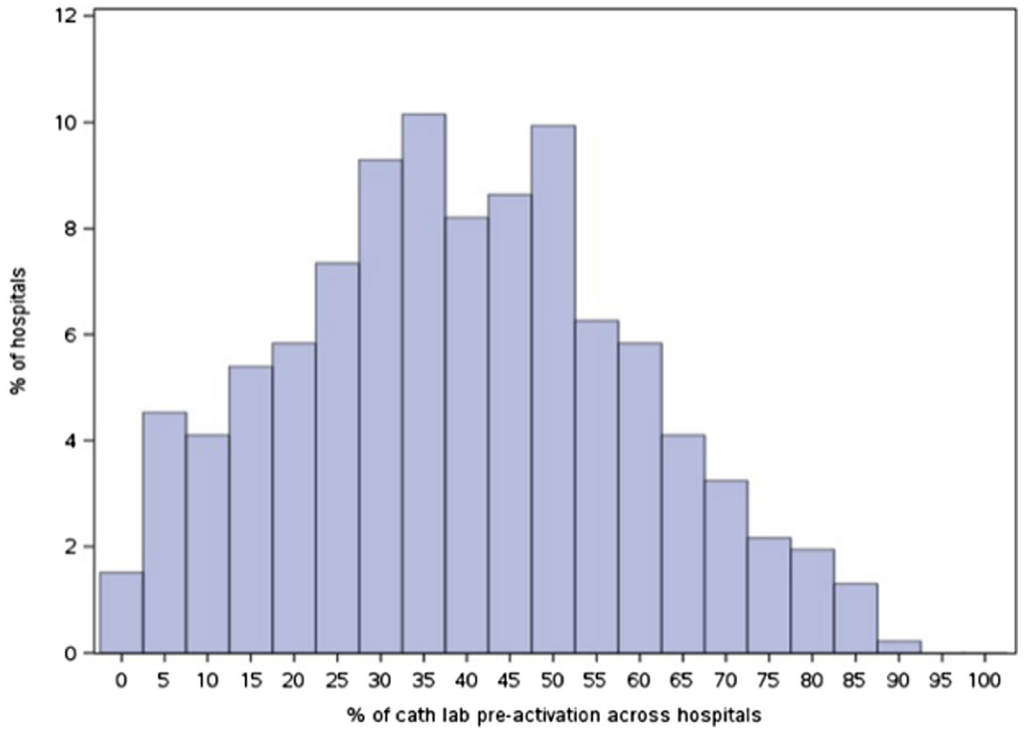


TABLE 3 Hospital Characteristics Stratified by Hospital-Level Tertiles of Cardiac Catheterization Laboratory Pre-Activation

		Hospital Tertiles by Catheterization Laboratory Pre-Activation			
	Overall	Low	Intermediate	High	p Value
Number of hospitals	463	153	155	155	
Pre-activation, %	0.0–88.9	0.0–29.7	30.0–47.9	48.0–88.9	
Hospital characteristics					
Region					0.38
West	15.8	19.0	12.3	16.1	
Northeast	13.2	11.8	16.8	11.0	
Midwest	24.0	24.2	26.5	21.3	
South	47.1	45.1	44.5	51.6	
Cardiothoracic surgery onsite	77.5	75.8	78.1	78.7	0.82
Academic teaching hospital*	17.9	22.2	20.0	11.6	0.040
Rural hospital	14.3	7.8	19.4	15.5	0.013
Annual STEMI volume, patients per yr	233 (157–355)	211 (127–298)	236 (163–346)	247 (168–435)	0.007
Defect-free care achieved, %	90.5 (78.1–95.2)	88.9 (74.1–95.8)	91.2 (80.0–95.5)	90.0 (80.0–94.5)	0.52

Values are % or median (interquartile range), unless otherwise indicated. *Membership in the Council of Teaching Hospitals.
STEMI = ST-segment elevation myocardial infarction.

note that catheterization laboratory activation occurred at any time prior to hospital arrival in approximately 75% of all pre-hospital-identified patients with STEMI, yet activation of the catheterization laboratory >10 min prior to hospital arrival occurs in only 41%. Every 10-min delay in notifying the receiving catheterization laboratory is associated with increasing door-to-device times. These findings highlight the importance of pre-activation timing relative to arrival at the receiving PCI center. Catheterization laboratory pre-activation is currently defined and measured simply by whether it occurred, regardless of its timing in relation to hospital arrival. Yet our results suggest that the amount of notification provided is important.

TABLE 4 Reperfusion Measures Stratified by Hospital-Level Tertiles of Cardiac Catheterization Laboratory Pre-Activation

	Overall (N = 25,037)	Low (n = 7,449)	Intermediate (n = 8,044)	High (n = 9,544)	p Value
Overall					
Door to device (min)	47 (35–59)	52 (40–64)	47 (35–60)	42 (31–55)	<0.001
FMC to device (min)	78 (65–92)	80 (67–95)	78 (65–93)	77 (64–90)	<0.001
FMC to device ≤90 min	72.2	68.9	71.8	75.2	<0.001
Off-hour presentation					
Door to device (min)	53 (42–64)	58 (48–69)	53 (43–65)	48 (38–59)	<0.001
FMC to device (min)	84 (73–98)	87 (75–100)	84 (73–99)	82 (71–95)	<0.001
FMC to device ≤90 min	63.4	58.3	62.5	68.0	<0.001
Work-hour presentation					
Door to device (min)	38 (29–49)	42 (33–53)	38 (29–48)	34 (25–45)	<0.001
FMC to device (min)	69 (57–82)	70 (58–83)	68 (57–82)	68 (57–82)	<0.001
FMC to device ≤90 min	84.4	83.2	84.7	85.1	0.07

Values are median (interquartile range) or %.
FMC = first medical contact.

Second, catheterization laboratory pre-activation was associated with significantly shorter reperfusion times for both work-hour and off-hour presentations. Contrary to the belief that pre-activating catheterization laboratories during work hours may have little meaningful time-to-treatment impact because the catheterization laboratory staff is already available onsite, our results highlight the importance of EMS pre-activating the catheterization laboratory across all presentation times. However, despite pre-activation, the majority of patients with STEMI continue to be first evaluated in the emergency department for both work-hour and off-hour presentations, with low rates of direct-to-catheterization laboratory transport. The necessity of processes such as patient registration, emergency department physician assessment, and repeat electrocardiography for STEMI confirmation that make an emergency department stop necessary need to be reevaluated to further reduce reperfusion delays (5,19).

Finally, we demonstrate that catheterization laboratory pre-activation is likely driven by needs that vary among regional STEMI systems of care. For instance, that the pre-activation group had longer FMC-to-hospital arrival times suggests that pre-activation was deemed critical in a setting in which transport to a PCI-capable center takes longer. Yet despite electrocardiograms' being acquired quickly after FMC, subsequent activation of the catheterization laboratory was delayed. This calls for an improved understanding of when catheterization laboratory activation occurs in the sequence of other pre-hospital processes, such as loading the patient

into the ambulance and pre-hospital medication administration.

At a system level, our results demonstrate that although catheterization laboratory pre-activation is used to some degree across most hospitals, its use varies substantially. Patients treated at hospitals with high pre-activation rates are associated with faster reperfusion times and lower in-hospital mortality than those treated at hospitals with intermediate and low rates of pre-activation. These findings likely reflect better coordination of STEMI care between EMS and high pre-activation PCI hospitals. In this respect, our findings align with the recently completed Mission: Lifeline Accelerator-2 endeavor, in which continuous feedback organized between hospital-EMS partnerships was associated with significantly improved regional reperfusion times and in-hospital survival (20). Collectively, these studies highlight that for catheterization laboratory pre-activation to provide a clinically meaningful impact on reperfusion delays in STEMI, a reasonable amount of catheterization laboratory notification is required. We use a 10-min notification window on the basis of clinical judgment that this would be the minimum amount of time needed to prepare a catheterization laboratory across hospital types. Shorter or longer time benchmarks could be considered, depending on geographic location, time of day, and proximity or anticipated delays to a PCI-capable hospital. Our findings importantly demonstrate a continuous relationship between the amount of notification provided and in-hospital reperfusion delays; this should be considered when establishing regional STEMI treatment protocols to maximize the time between pre-activation and hospital arrival. Further research within other large and global STEMI networks is required to define and validate the optimal time window for pre-activation to facilitate timely reperfusion.

STUDY LIMITATIONS. First, hospital participation within the ACTION Registry is voluntary, and participating hospitals may differ from nonparticipating hospitals in their patient and hospital profiles. However, our study represents hospitals from multiple geographic regions, enhancing the generalizability of our findings.

Second, within the observational context of our dataset, unmeasured confounding exists, and its impact on reperfusion times and clinical outcomes is unaccounted for. For instance, the physical distance between FMC and the primary PCI center has not been considered in evaluating the time-to-treatment relationships. However, considering that 90% of Americans live within 60 min of a PCI center (21,22), we believe our findings should be largely applicable across most nationwide STEMI networks. Additionally, accurate information on the use and timing of pre-hospital antithrombotic agents is not available within the dataset, but it would have been interesting to evaluate their relationship with pre-activation and patient outcomes.

Third, regional differences in pre-activation protocols, EMS capabilities, and catheterization laboratory activation processes and their influence on reperfusion timing and clinical outcomes could not be comprehensively evaluated within our analysis. Patient-specific information relating to medically necessary delays within the emergency department, such as a need to exclude an alternative, competing diagnosis or a need for medical stabilization prior to catheterization laboratory transfer, could also not be accurately ascertained.

Finally, the ACTION Registry does not collect information pertaining to catheterization laboratory activations for patients initially but not ultimately diagnosed with STEMI. Therefore, the impact of false catheterization laboratory activations on patient outcomes and overall resource use is not profiled in this analysis.

CONCLUSIONS

Fewer than one-half of EMS-transported patients with STEMI arrived at PCI centers that had been pre-activated, with wide variability in this practice noted across primary PCI hospitals in the United States. Patients treated at hospitals with higher rates of catheterization laboratory pre-activation had shorter reperfusion times and lower in-hospital mortality than those treated at hospitals that were infrequently pre-activated. Our results highlight opportunities to optimize the implementation of this pre-hospital process of STEMI care.

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PERSPECTIVES

WHAT IS KNOWN? Pre-hospital cardiac catheterization laboratory activation is a key process of STEMI care. For patients with STEMI diagnosed in the pre-hospital setting, little is known on how this advanced notification associates with primary PCI-related reperfusion delays and in-hospital outcomes.

WHAT IS NEW? The use of pre-hospital cardiac catheterization laboratory activation in contemporary practice is modest and varies widely across PCI-capable hospitals. This strategy is, however, associated in a time-dependent manner with shorter reperfusion times and possibly lower in-hospital mortality.

WHAT IS NEXT? Aligned with other time-sensitive standards in STEMI care, opportunities to better define and optimize the implementation of this pre-hospital process of STEMI care are identified.

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KEY WORDS pre-hospital cardiac catheterization laboratory activation, primary percutaneous coronary intervention, ST-segment elevation myocardial infarction

APPENDIX For supplemental tables, please see the online version of this paper.